Attributes of Exemplary Research

Negotiating for Success: Navigating the Contracting Process for an Exemplary Research Program

By Allison R. Baer, RN, BSN, John A. Hohneker, MD, Teresa L. Stewart, MHA, and Claire F. Verschraegen, MD

American Society of Clinical Oncology, Alexandria, VA; Novartis Pharmaceuticals Corporation, East Hanover, NJ; New Mexico Cancer Care Alliance; University of New Mexico Cancer Center Clinical Trials Office; and University of New Mexico Cancer Research and Treatment Center, Albuquerque, NM

Effectively negotiating contracts is essential to ensuring the overall success of sites that conduct clinical trials. This article, part of the Attributes of Exemplary Research series,[1] incorporates practical advice from experts and discusses negotiation tips helpful for every clinical research site.

Contracting Basics

Successful contracting is imperative for research sites that conduct company-sponsored or investigator-initiated clinical trials. Good contracts help ensure the sustainability of a site and guide how research will be conducted at the site. A contract should include both basic and high-level issues, including protection of patient confidentiality, intellectual property rights, and reimbursement provisions. Because responsibilities listed in the contract may not be included in the protocol, it is important that research staff read both.

Because of the perceived complexity of contracts, some investigators delegate this task to a legal team. Although legal counsel can determine if a contract contains appropriate legal language, only the investigators can determine if the study is compelling and achievable at the site. For greatest efficiency, one research staff member at the site should be designated to oversee the contracting process and serve as point of contact. This person ensures that negotiations are conducted in a timely manner, verifies that site-specific needs are addressed, and communicates with any third parties that may be involved. Development and use of standard operating procedures (SOPs) guide staff through the process and ensure that all tasks are completed in a smooth and consistent manner.[2]

It is also important to understand the various types of contracts and know if the trial sponsor permits negotiation. For example, some federally sponsored trials, such as those offered through the National Cancer Institute (NCI) Cooperative Group system, generally offer little room for negotiation. With limited ability to negotiate, the site must compare both positive and negative elements in the contract and verify that the trial is both achievable at the site and feasible under the allotted budget. On the contrary, contracts for privately sponsored trials, such as those sponsored by pharmaceutical companies, are usually open for negotiation. Elements deemed undesirable by the research site may be negotiated with the sponsor in an attempt to reach a mutually agreeable conclusion. Investigator-initiated trials require a third approach. In this situation, the investigator is generally involved in the initial preparation of the contract, which requires the site to be more proactive. Trial sponsors usually provide templates the investigator should follow; if not, a previous contract from the sponsor can serve as a starting point. Using a standard form expedites the process for both parties.

Standard Terminology

Most sponsors aim to start recruitment at a site within 3 to 4 months of initial contact about the trial, but negotiating a contract can potentially delay this timeline. In recognition of this problem, the NCI convened a working group of representatives from the CEO Roundtable on Cancer Life Sciences Consortium and several NCI-designated cancer centers. The group developed the Standard Terms of Agreement for Research Trial (START) clauses, which outline standard language commonly used in research agreements.[3] Development of standard language aims to reduce the length of time it takes parties to negotiate contracts, thus saving money and reducing trial initiation time.

The START clauses, which can be downloaded free,[4] focus on the two types of contracts most commonly negotiated: company-sponsored trials and investigator-initiated trials. On the basis of the differing needs of these two types of contracts, the START clauses are divided into two sections that include standard language specific to each circumstance. The standard language in both sections focus on six key areas most commonly addressed in a clinical trial contract: intellectual property, study data, indemnification, subject injury, confidentiality, and publication rights. If a research site is creating a contract or wants to verify that the terminology used in a contract is accurate, the START clauses serve as a helpful resource (Fig 1).[4]

Reimbursement procedures should be clearly identified in the contract, although the budget itself is often included as an appendix. When verifying that reimbursement is adequate, a site should compare its fee schedule with the pro-

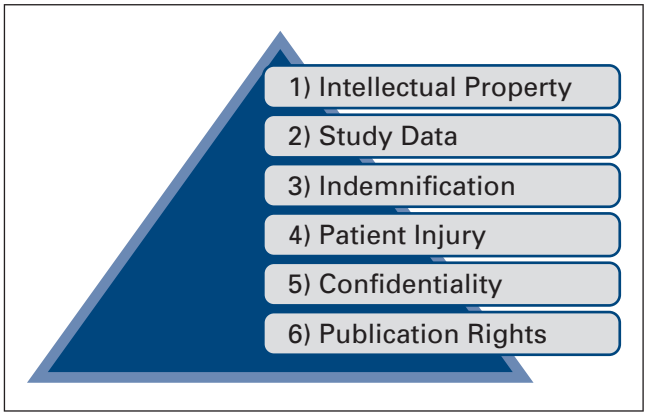

Figure 1. Major elements of a clinical research contract. Data adapted.[4]

posed budget. For example, if the protocol requires a radiology scan that is not standard of care, research personnel can expeditiously compare the proposed budget with the fee schedule to determine if the reimbursement will be adequate. If the site does not have an established fee schedule, invoices used to bill insurance companies can be a helpful starting point. Sponsors prefer working with sites that have a good handle on their costs, and accurate fee schedules facilitate this. Also important to address in the contract are whether payments are made at the time of expense, at the end of the study, or according to a combination of both; whether startup costs are reimbursed; and whether the sponsor sends payments automatically on the basis of case report forms or if invoices are required. If invoices are required, it is important to know exactly to whom they should be sent.

Although a contract is always important, it becomes especially vital when things are not going as planned. During the initial contracting process, sites must consider worst-case scenarios and be sure the contract guarantees the protection of the site in situations that—it is hoped—never arise. For example, provisions regarding patient injury are important and should outline who is financially responsible for complications related to the study drug. Research agreements may also include minimum or maximum accrual objectives, and the site must be realistic about its commitment to enroll a designated number of patients. Depending on the type of trial, intellectual property and publication rights are also essential. Using a checklist that identifies all major elements of a contract is a useful way to confirm that all required elements are included. When assembling the checklist, compile basic elements of the contract listed above and any site-specific requirements, such as laws or policies specific to the state, research site, or population being studied. It is worthwhile to dedicate time to making a complete checklist that considers all factors that must be addressed in the contract. A thorough list is an excellent way to ensure all required elements are included in the contract and will be a helpful template for future contracts negotiated at the research site.

ASCO Statement on Minimum Standards and Exemplary Attributes of Clinical Trial Sites

The ASCO statement addresses the minimum requirements for sites conducting quality clinical trials as well as the attributes of exemplary sites. Both minimum requirements and exemplary attributes were developed based on a review of the literature, current regulatory requirements, and consensus among community and academic clinical researchers. To conduct quality clinical research, sites should meet the minimum requirements. It should be noted, however, that the exemplary attributes are voluntary and suggested as goals, not requirements. Not all attributes will apply to all clinical trial sites, and many sites may be able to conduct high-quality clinical trials without possessing all attributes.

Party to the Contract

Deciding who will be the party to sign the contract is a complex decision. As indicated in the START clauses, both the research institution and principal investigator can be listed as parties on the contract. However, if the sponsor and research institution agree, a principal investigator employed by the research site is not required to be a party.[4] In the latter case, the institution is the designated party on the contract, but under federal regulations, the principal investigator still assumes legal liability for appropriate research conduct on the basis of the US Food and Drug Administration (FDA) Form 1572, which he or she must sign regardless of who signs the contract, provided the study is being submitted to the FDA.[5] Specific liability of the investigator is generally outlined in the research agreement as well. It is important to know the sponsor's guidelines, because sometimes the sponsor actually prefers that the principal investigator not sign the contract unless he or she is a legal delegate for the institution. Either way, having as few signatures as possible reduces time and confusion when amendments are needed.

When the option to sign is given to the investigator, he or she should weigh the decision carefully. As mentioned, some investigators do not sign contracts to protect themselves from legal liability beyond what is assumed by the FDA Form 1572. However, if an investigator is not the party designated on the contract, he or she may face certain limits. For example, if the investigator is not a party on the contract and moves to a different institution, he or she may not have authorization to relocate the study. This can be particularly concerning in the situation of investigator-initiated trials, because the institution, not the investigator, holds the intellectual property and publication rights. Understanding the policies of the sponsor and research site is imperative when making this decision.

Negotiating

After discussing the contract at the research site, the next step is negotiating. To assure a smooth negotiation process, the research site must prepare in advance of discussion with the spon-

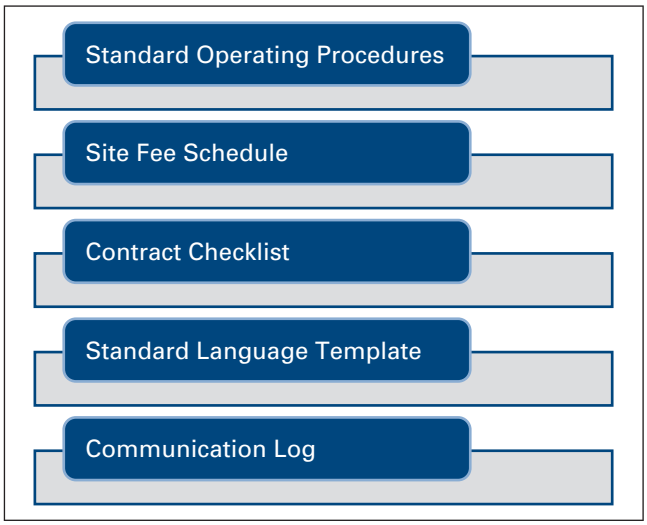

Figure 2. Suggested templates to assist with negotiating a contract.

sor. In addition to reading and understanding the contract, initial preparation should involve understanding the needs of all stakeholders involved. Understanding the perspective of the sponsor can be advantageous and worthwhile. Does the sponsor recognize the site for consistently conducting reliable research? Does the site work efficiently during the negotiation process, indicating that it will initiate the protocol in a reasonable period of time? Having a realistic understanding of sponsor's position can provide empowering information.

It is important to determine what elements, if any, require negotiation. If several elements are identified, they should be ranked in order of importance, from items that must be modified for the site to offer the trial to smaller details that may be acceptable if not modified. Be prepared to provide documentation that supports why items are being negotiated. Sponsors reimburse at fair market value, so if sites request additional funding, they should be able to submit proof verifying why there are additional costs. Sponsors understand that regional and geographic differences exist but need documentation on file.

Because reducing trial initiation time is of utmost importance, finding ways to expedite the process is useful. For example, submitting the trial for institutional review board approval while concurrently negotiating the contract (if permitted) can reduce initiation time by weeks. Smaller efforts can make a big difference as well. If the research site wants to make a revision to the contract, drafting exact wording for the revisions is much more efficient than simply stating the problem and expecting the sponsor to draft the language. A consistent and efficient approach is to maintain a document that lists standard language commonly used by the site. For instance, if the site frequently conducts trials that require storage of tissue specimens but does not have processing facilities on site, standard language that indicates how this issue will be addressed should be created. Additionally, if the negotiation is being conducted electronically, be sure to make modifications using the track-changes feature for easy identification by the sponsor. This helps the sponsor quickly identify the proposed modifications and fosters an honest and transparent relationship between both parties. If electronic communication, such as e-mail, is not providing a timely and mutually agreeable outcome, never hesitate to call the other party, negotiate by phone, and follow up in writing. It is often less time consuming to speak by phone than to fumble through an endless chain of e-mails. Once a relationship is established, the sponsor may be willing to develop a master contract that incorporates the site-specific needs.

No matter which communication method is chosen, maintaining a communication log is essential. The log should include the name and contact information of every individual involved. This log is especially helpful when there is a discrepancy regarding items that have been agreed on or when more than one person is completing negotiations, such as when the primary contact goes on vacation, or the negotiations require a discussion with higher-level personnel. Documenting a synopsis of every discussion, including any changes that have already been agreed on, can save time and facilitate future communications. Whether negotiating electronically or by phone, both parties should strive to designate one point of contact who can negotiate through the whole process.

The process of negotiating does not need to be daunting. Conducting negotiations in a professional and timely manner is imperative, and as long as the site is being realistic, the sponsor is generally willing to make modifications. Remember that both parties are working toward the same goal: to initiate the trial. Sponsors want sites that conduct high-quality research, and it is the responsibility of the site to verify that this objective will be met under the terms of the contract. Implementation of the strategies and templates (Fig 2) discussed in this article can improve efficiency and contribute to an exemplary research program.

Upcoming Events

ASCO plans to offer online educational opportunities, in which content providers to the series will discuss these topics in more detail. Visit ASCO's Web site at www.asco.org/ClinicalTrialResources for more information, and access the entire Attributes of Exemplary Research series at http://jop.ascopubs.org. The next article in this series, which focuses on biospecimens and biomarkers, will be published in an upcoming issue of *Journal of Oncology Practice*.

Feedback Request

Suggest future topic ideas for the series and provide your feedback by sending an e-mail to researchresources@asco.org.

Accepted for publication on January 7, 2010.

Acknowledgment

We thank Lisa Johnson, RN, BSN, for providing helpful content and feedback for this article. The information contained in this article is

general in nature. It is not intended to be, and should not be construed as, legal advice relating to any particular situation.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

Author Contributions

Conception and design: Allison R. Baer

Administrative support: Allison R. Baer

Collection and assembly of data: Allison R. Baer

Manuscript writing: Allison R. Baer, Claire F. Verschraegen

Final approval of manuscript: Allison R. Baer, John A. Hohneker, Teresa L. Stewart, Claire F. Verschraegen

Corresponding author: Allison R. Baer, RN, BSN, Department of Research Policy, American Society of Clinical Oncology, 2318 Mill Rd, Ste 800, Alexandria, VA 22314; e-mail: Allison.Baer@asco.org.

DOI: 10.1200/JOP.091082

References

1. Zon R, Meropol NJ, Catalano RB, et al: American Society of Clinical Oncology Statement on minimum standards and exemplary attributes of clinical trial sites. J Clin Oncol 26:2562-2567, 2008

2. Good clinical practice research guidelines reviewed, emphasis given to responsibilities of investigators: Second article in a series. J Oncol Pract 4:233-235, 2008

3. National Cancer Institute: Restructuring the NCI Clinical Trials Enterprise: START Clauses. http://restructuringtrials.cancer.gov/initiatives/standardization/highlights/start

4. National Cancer Institute, CEO Roundtable on Cancer: Proposed Standardized/Harmonized Clauses for Clinical Trial Agreements. http://restructuringtrials.cancer.gov/files/StClauses.pdf

5. US Department of Health and Human Services: US Food and Drug Administration: FDA Forms. http://www.fda.gov/aboutfda/reportsmanualsforms/forms/default.htm

ERRATUM

The January article by Nevidjon et al, entitled "Filling the Gap: Development of the Oncology Nurse Practitioner Workforce" (J Oncol Pract 6:2-6, 2010), contained an error in the corresponding author's e-mail address. It was originally published as mmcorkle@ons.org, whereas it should have been mmccorkle@ons.org. The online version has been corrected in departure from the print. *Journal of Oncology Practice* apologizes to the authors and readers for the mistake.

DOI: 10.1200/JOP.091091